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| 09/469,812 | 12/22/1999 | MAARTEN H. STUIVER | SYN-014 | 5404 |

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Hale and Dorr LLP
60 State Street
Boston, MA 02109

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| EXAMINER |
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KRUSE, DAVID H

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| ART UNIT | PAPER NUMBER |
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1638

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DATE MAILED: 10/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/469,812

Applicant(s)

STUIVER ET AL.

Examiner

David H Kruse

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 August 2001 and 23 August 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,4-6 and 8-11 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,4-6 and 8-11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

STATUS OF THE APPLICATION

1. This Office action is in response to the Amendments filed 28 August 2001 and 23 August 2002.
2. The Supplemental Amendment filed 23 August 2002, requesting entry of new claim 12, has not been entered in view of the petition decision mailed 17 July 2002 from the Office of Petitions and Applicant's failure to respond to the proposed copy claim within the time limit set forth in the Office action mailed 28 March 2001.
3. Those rejections not specifically addressed in this Office action are withdrawn in view of Applicant's amendments and/or arguments filed 28 August 2001.
4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Drawings

5. The drawings in this application are objected to by the Draftsperson as informal. See the PTO-948 form attached to the Office action mailed 28 March 2001. Applicant is reminded that correction of the drawings cannot be held in abeyance, and that formal drawings are required in response to this Office Action as outlined in 37 CFR § 1.85(a). Failure to take corrective action within the set period will be considered non-responsive to this Office action.

Sequence Compliance

6. Claim 5 fails to comply with 37 CFR § 1.821(c) because said claim discloses a nucleic acid sequence but does not have a SEQ ID NO identifier in the claim. Applicant

is required to insert -- (SEQ ID NO: 19) -- after the recitation of the nucleic acid sequence at line 2 of the claim.

Claim Objections

7. Claim 2 is objected to because of the following informalities: The listing of species in the Markush groups should be delineated with the conjunction -- and -- after "toxin," at line 2 and after "dicarboxylate translocator gene," at line 6. In addition, at lines 5 and 6, the recitation of "dicarboxylate translocator gene" appears twice, one instance must be deleted. Appropriate correction is required.
8. Claim 2 is objected to under 37 CFR § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Specifically, claim 2 is broader in scope than claim 1 which recites "a gene encoding a toxin gene and/or a nucleotide that interferes with DNA unwinding", where claim 2 recites "and an antisense sequence for a housekeeping gene" which Applicant does not define as falling within the scope of "a toxin gene" or "a nucleotide that interferes with DNA unwinding" in the specification (see pages 4-9 of the specification).
9. Claim 10 is objected to under 37 CFR § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. In the instant case, the

limitation "the host is a member of the Agrobacteriaceae" fails to further limit the "plant host" of claim 9. Appropriate correction is required.

Claim Rejections - 35 USC § 112

10. Claims 1, 4, 6 and 8-11 remain rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant claims a vector for plant transformation comprising a T-DNA sequence comprising a sequence located between two direct repeats and a gene encoding a toxin gene and/or a nucleotide sequence that interferes with DNA unwinding, wherein said nucleotide sequence that interferes with DNA unwinding is a sequence which binds a DNA binding protein or wherein said nucleotide sequence that interferes with DNA unwinding is a sequence of 20-60 basepairs with a GC-content of more than 80%. Applicant claims method of transforming a plant cell using said vector and a plant host and an Agrobacteriaceae host comprising said vector.

Applicant describes a vector comprising a barnase encoding DNA sequence, a GC clamp sequence comprising SEQ ID NO: 5 and 6, or a DNA sequence to which Vir G binds, to the left of the T-DNA left border sequence, a method of using said vector and a plant cell comprising said vector.

Applicant does not describe the genus of genes encoding a toxin or nucleotide sequences that interfere with DNA unwinding required to make a vector and practice the

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methods as broadly claimed. The instant claims are directed to a vector and methods of using same comprising a nucleotide sequence that is only described by function.

See also, MPEP § 2163 which states that the claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence.

11. Claims 1, 2, 4, 5, 6 and 8-11 remain rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for a vector comprising a barnase encoding DNA sequence, a GC clamp sequence comprising SEQ ID NO: 5 and 6, or a DNA sequence to which Vir G binds, to the left of the T-DNA left border sequence, a method of using said vector and a plant cell comprising said vector, does not reasonably provide enablement for a vector comprising a DNA sequence to the left of the T-DNA left border sequence encoding any toxic compound, any GC rich DNA sequence, or a sequence to which any DNA-binding protein interacts, a method of using said vector or a plant cell comprising said vector. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. This rejection is repeated for the reason of record as set forth in the last Office action mailed 28 March

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2001. Applicant's arguments filed 28 August 2001 have been fully considered but they are not persuasive.

Applicant argues that Applicant is not required to disclose every species encompassed by a claim even in an unpredictable art (pages 12-13 of the Remarks). This argument is not found to be persuasive because the instant claims do not designate where the toxin and/or the nucleotide sequence that interferes with DNA unwinding is in relation to the sequence located between two direct repeats is/are. In addition, Applicant does not teach how to make and use the genus of sequences at claim 4 that binds a DNA binding protein or at claim 6 which interfere with DNA unwinding, either of which would be required to make and use the vector at claim 1. At claim 2, Applicant has not taught how to make and use the genus of antisense sequences for housekeeping genes without undue trial and error experimentation because the sequence for each species of plant for each housekeeping gene of each the groups of genes would have had to have been isolated and sequence to produce each vector to practice the method of either of claim 8 or 11.

See *In re Fisher*, 166 USPQ 18, 24 (CCPA 1970) which teaches "That paragraph (35 USC 112, first) requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art. In cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws. In cases

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involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.” In the instant case, Applicant invites undue trial and error experimentation by one of skill in the art, especially as directed to any toxin gene or any nucleotide sequence that interferes with DNA unwinding.

12. Claims 1, 2, 4, 6 and 8-11 remain rejected and claim 5 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is repeated for the reason of record as set forth in the last Office action mailed 28 March 2001. Applicant's arguments filed 28 August 2001 have been fully considered but they are not persuasive.

At claim 1, it remains unclear where “a gene encoding a toxin gene and/or a nucleotide sequence that interferes with DNA unwinding” is located in relation to “a sequence located between two direct repeats” within the claimed vector. Hence, it remains unclear what the metes and bounds of the invention are. Consequently, claims 2, 4-6 and 8-11 are also indefinite because they do not clarify the metes and bounds of the claimed invention. Applicant's statement that claim 1 has been amended to more clearly distinguish the relationship between genes encoded by the vector is not found to be persuasive, the rejection remains (page 13 of the Remarks).

At claim 11, line 2, the phrase “the transformed cell” lacks proper antecedent basis within the claim, and should read -- a transformed plant cell --.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(g)(1) during the course of an interference conducted under section 135 or section 291, another inventor involved therein establishes, to the extent permitted in section 104, that before such person's invention thereof the invention was made by such other inventor and not abandoned, suppressed, or concealed, or (2) before such person's invention thereof, the invention was made in this country by another inventor who had not abandoned, suppressed, or concealed it. In determining priority of invention under this subsection, there shall be considered not only the respective dates of conception and reduction to practice of the invention, but also the reasonable diligence of one who was first to conceive and last to reduce to practice, from a time prior to conception by the other.

14. Claims 1, 2, 8 and 11 are rejected under 35 U.S.C. § 102(g) as being anticipated by Gutterson *et al* (U.S. Patent No. 6,521,458, filed 30 April 1999, which claims benefit of U.S. Provisional Application 60/086,440, filed 22 May 1998).

Applicant failed to respond to the proposed copy claim for the purpose of interference put forth in the Office action mailed 28 March 2001. Applicant's petition for waiver of the one-month time limit to respond to the copy claim required under 37 CFR § 1.605(a) in the petition filed under 37 CFR § 1.183, filed 7 June 2002, was denied by the Office of Petitions in the response mailed 17 July 2002. Failure to present claims and/or take necessary steps for interference purposes after notification that interfering subject matter is claimed constitutes a disclaimer of the subject matter. This amounts to a concession that, as a matter of law, the patentee is the first inventor in this country. See *In re Oguie*, 517 F.2d 1382, 186 USPQ 227 (CCPA 1975).

U.S. Patent No. 6,521,458, Gutterson *et al*, discloses a vector and a method of using said vector for producing a transgenic plant wherein said vector comprises a polynucleotide of interest comprising a T-DNA sequence with a polynucleotide

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sequence encoding a lethal polypeptide located beyond the left T-DNA border (claim 1), wherein said lethal peptide is the ribonuclease Barnase (claim 3), and an isolated T-DNA vector comprising a lethal polynucleotide sequence encoding a lethal polypeptide located beyond the left T-DNA border (claim 8). Hence, Gutterson *et al* had previously disclosed all of the claim limitations.

Claim Rejections - 35 USC § 103

15. Claims 1, 2 and 8-11 are rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,421,458, filed 30 April 1999, Gutterson *et al*.

Applicant failed to respond to the proposed copy claim for the purpose of interference put forth in the Office action mailed 28 March 2001 is outlined above. Failure to present claims and/or take necessary steps for interference purposes after notification that interfering subject matter is claimed constitutes a disclaimer of the subject matter. This amounts to a concession that, as a matter of law, the patentee is the first inventor in this country. See *In re Oguie*, 517 F.2d 1382, 186 USPQ 227 (CCPA 1975).

The teachings of Gutterson *et al* are outlined above.

Gutterson *et al* do not specifically claim a plant host or an Agrobacteriaceae host comprising the taught vector outlined above.

The method and vector taught by Gutterson *et al* as outlined above renders obvious the plant host and host of the Agrobacteriaceae of claims 9 and 10 respectively because said plant host and Agrobacteriaceae host would be obvious final and

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intermediate products of the method taught by Gutterson *et al* (see Example 4 at columns 15-18).

16. Claims 1, 4, 5 and 9-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ramanathan *et al* (Plant Molecular Biology 1995, 28: 1149-1154) in view of D'Souza-Ault *et al* (1993, J. Bacteriology 175(11): 3486-3490).

The teachings of Ramanathan *et al* can be found in the previous Office action. In addition Ramanathan *et al* teach that it would be desirable to incorporate into a T-DNA vectors a 'stop-transfer' signal adjacent to the left border (paragraph spanning pages 1152-1153). The vector taught by Ramanathan *et al* comprises a sequence located between two direct repeats, and Ramanathan *et al* teaches of method of transforming plants and obtaining transgenic plants (see page 1151).

Ramanathan *et al* does not specifically teach a vector comprising a vir box sequence to which a transcriptional repressor binds.

D'Souza-Ault *et al* teach the vir box consensus sequence and that VirG can act as a repressor blocking the transcription of upstream sequences from the vir box (page 3489).

Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the vector for transforming plants taught by Ramanathan *et al* to incorporate a vir box binding sequence beyond the left T-DNA border as taught by D'Souza-Ault *et al* to incorporate a 'stop-transfer' signal adjacent to the left border as suggested by Ramanathan. It would have been obvious to use the modified vector in a method of transforming plant cells and producing transgenic plants.

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One of ordinary skill in the art would have had a reasonable expectation of success in producing a modified vector given the teachings of both Ramanathan *et al* and D'Souza-Ault *et al*, and given the relative skill in the art at the time of Applicant's invention.

Conclusion

17. Claim 6 is free of the prior art, which neither teaches nor fairly suggest a vector comprising a T-DNA sequence and a nucleotide sequence that interferes with DNA unwinding of 20-60 base-pairs with a GC content of more than 80%.
18. No claims are allowed.
19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David H. Kruse, Ph.D. whose telephone number is (703) 306-4539. The examiner can normally be reached on Monday to Friday from 8:00 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Amy Nelson can be reached at (703) 306-3218. The fax telephone number for this Group is (703) 872-9306 Before Final or (703) 872-9307 After Final.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group Receptionist whose telephone number is (703) 308-0196.



David H. Kruse, Ph.D.
22 September 2003